

# SEQUENCE LISTING

<110> Baxter, John  
Fletterick, Robert  
Kushner, Peter

<120> NUCLEAR RECEPTOR LIGANDS AND LIGAND BINDING DOMAINS

<130> UCAL-246/02/1US

<140> Not Yet Available

<141> 2000-08-10

<150> US 08/980,115

<151> 1997-11-26

<150> US 08/764,870

<151> 1996-12-13

<150> US 60/008,606

<151> 1995-12-14

<150> US 60/008,543

<151> 1995-12-13

<150> US 60/008,540

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<170> PatentIn version 3.0

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<212> PRT

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<222> (157)..(410)

<223> minimal ligand binding domain

<220>

<221> DOMAIN

<222> (393)..(405)

<223> activation domain

<400> 1

Met Glu Gln Lys Pro Ser Lys Val Glu Cys Gly Ser Asp Pro Glu Glu  
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Asn Ser Ala Arg Ser Pro Asp Gly Lys Arg Lys Arg Lys Asn Gly Gln  
20 25 30

Cys Pro Leu Lys Ser Ser Met Ser Gly Tyr Ile Pro Ser Tyr Leu Asp  
 35 40 45  
 Lys Asp Glu Gln Cys Val Val Cys Gly Asp Lys Ala Thr Gly Tyr His  
 50 55 60  
 Tyr Arg Cys Ile Thr Cys Glu Gly Cys Lys Gly Phe Phe Arg Arg Thr  
 65 70 75 80  
 Ile Gln Lys Asn Leu His Pro Thr Tyr Ser Cys Lys Tyr Asp Ser Cys  
 85 90 95  
 Cys Val Ile Asp Lys Ile Thr Arg Asn Gln Cys Gln Leu Cys Arg Phe  
 100 105 110  
 Lys Lys Cys Ile Ala Val Gly Met Ala Met Asp Leu Val Leu Asp Asp  
 115 120 125  
 Ser Lys Arg Val Ala Lys Arg Lys Leu Ile Glu Gln Asn Arg Glu Arg  
 130 135 140  
 Arg Arg Lys Glu Glu Met Ile Arg Ser Leu Gln Gln Arg Pro Glu Pro  
 145 150 155 160  
 Thr Pro Glu Glu Trp Asp Leu Ile His Val Ala Thr Glu Ala His Arg  
 165 170 175  
 Ser Thr Asn Ala Gln Gly Ser His Trp Lys Gln Arg Arg Lys Phe Leu  
 180 185 190  
 Pro Asp Asp Ile Gly Gln Ser Pro Ile Val Ser Met Pro Asp Gly Asp  
 195 200 205  
 Lys Val Asp Leu Glu Ala Phe Ser Glu Phe Thr Lys Ile Ile Thr Pro  
 210 215 220  
 Ala Ile Thr Arg Val Val Asp Phe Ala Lys Lys Leu Pro Met Phe Ser  
 225 230 235 240  
 Glu Leu Pro Cys Glu Asp Gln Ile Ile Leu Leu Lys Gly Cys Cys Met  
 245 250 255  
 Glu Ile Met Ser Leu Arg Ala Ala Val Arg Tyr Asp Pro Glu Ser Asp  
 260 265 270  
 Thr Leu Thr Leu Ser Gly Glu Met Thr Val Lys Arg Lys Gln Leu Lys  
 275 280 285  
 Asn Gly Gly Leu Gly Val Val Ser Asp Ala Ile Phe Glu Leu Gly Lys  
 290 295 300  
 Ser Leu Ser Ala Phe Asn Leu Asp Asp Thr Glu Val Ala Leu Leu Gln  
 305 310 315 320  
 Ala Val Leu Leu Met Ser Thr Asp Arg Ser Gly Leu Leu Cys Val Asp  
 325 330 335

Lys Ile Glu Lys Ser Gln Glu Ala Tyr Leu Leu Ala Phe Glu His Tyr  
 340 345 350

Val Asn His Arg Lys His Asn Ile Pro His Phe Trp Pro Lys Leu Leu  
 355 360 365

Met Lys Val Thr Asp Leu Arg Met Ile Gly Ala Cys His Ala Ser Arg  
 370 375 380

Phe Leu His Met Lys Val Glu Cys Pro Thr Glu Leu Phe Pro Pro Leu  
 385 390 395 400

Phe Leu Glu Val Phe Glu Asp Gln Glu Val  
 405 410

<210> 2  
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 <213> Homo sapiens

<220>  
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 <222> (157)..(410)  
 <223> minimal ligand binding domain

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Met Glu Gln Lys Pro Ser Lys Val Glu Cys Gly Ser Asp Pro Glu Glu  
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Asn Ser Ala Arg Ser Pro Asp Gly Lys Arg Lys Arg Lys Asn Gly Gln  
 20 25 30

Cys Ser Leu Lys Thr Ser Met Ser Gly Tyr Ile Pro Ser Tyr Leu Asp  
 35 40 45

Lys Asp Glu Gln Cys Val Val Cys Gly Asp Lys Ala Thr Gly Tyr His  
 50 55 60

Tyr Arg Cys Ile Thr Cys Glu Gly Cys Lys Gly Phe Phe Arg Arg Thr  
 65 70 75 80

Ile Gln Lys Asn Leu His Pro Thr Tyr Ser Cys Lys Tyr Asp Ser Cys  
 85 90 95

Cys Val Ile Asp Lys Ile Thr Arg Asn Gln Cys Gln Leu Cys Arg Phe  
 100 105 110

Lys Lys Cys Ile Ala Val Gly Met Ala Met Asp Leu Val Leu Asp Asp  
 115 120 125

Ser Lys Arg Val Ala Lys Arg Lys Leu Ile Glu Gln Asn Arg Glu Arg  
 130 135 140

Arg Arg Lys Glu Glu Met Ile Arg Ser Leu Gln Gln Arg Pro Glu Pro  
 145 150 155 160

Thr	Pro	Glu	Glu	Trp	Asp	Leu	Ile	His	Ile	Ala	Thr	Glu	Ala	His	Arg	
				165					170					175		
Ser	Thr	Asn	Ala	Gln	Gly	Ser	His	Trp	Lys	Gln	Arg	Arg	Lys	Phe	Leu	
			180					185					190			
Pro	Asp	Asp	Ile	Gly	Gln	Ser	Pro	Ile	Val	Ser	Met	Pro	Asp	Gly	Asp	
		195					200					205				
Lys	Val	Asp	Leu	Glu	Ala	Phe	Ser	Glu	Phe	Thr	Lys	Ile	Ile	Thr	Pro	
	210					215					220					
Ala	Ile	Thr	Arg	Val	Val	Asp	Phe	Ala	Lys	Lys	Leu	Pro	Met	Phe	Ser	
225					230					235					240	
Glu	Leu	Pro	Cys	Glu	Asp	Gln	Ile	Ile	Leu	Leu	Lys	Gly	Cys	Cys	Met	
			245						250					255		
Glu	Ile	Met	Ser	Leu	Arg	Ala	Ala	Val	Arg	Tyr	Asp	Pro	Glu	Ser	Asp	
			260					265					270			
Thr	Leu	Thr	Leu	Ser	Gly	Glu	Met	Ala	Val	Lys	Arg	Glu	Gln	Leu	Lys	
		275					280						285			
Asn	Gly	Gly	Leu	Gly	Val	Val	Ser	Asp	Ala	Ile	Phe	Glu	Leu	Gly	Lys	
	290					295					300					
Ser	Leu	Ser	Ala	Phe	Asn	Leu	Asp	Asp	Thr	Glu	Val	Ala	Leu	Leu	Gln	
305					310					315					320	
Ala	Val	Leu	Leu	Met	Ser	Thr	Asp	Arg	Ser	Gly	Leu	Leu	Cys	Val	Asp	
				325					330					335		
Lys	Ile	Glu	Lys	Ser	Gln	Glu	Ala	Tyr	Leu	Leu	Ala	Phe	Glu	His	Tyr	
			340					345					350			
Val	Asn	His	Arg	Lys	His	Asn	Ile	Pro	His	Phe	Trp	Pro	Lys	Leu	Leu	
		355					360					365				
Met	Lys	Val	Thr	Asp	Leu	Arg	Met	Ile	Gly	Ala	Cys	His	Ala	Ser	Arg	
		370				375					380					
Phe	Leu	His	Met	Lys	Val	Glu	Cys	Pro	Thr	Glu	Leu	Phe	Pro	Pro	Leu	
385					390					395					400	
Phe	Leu	Glu	Val	Phe	Glu	Asp	Gln	Glu	Val							
				405					410							

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 <212> PRT  
 <213> Homo sapiens  
  
 <220>  
 <221> DOMAIN  
 <222> (211)..(461)

<223> minimal ligand binding domain

<400> 3

Met Thr Pro Asn Ser Met Thr Glu Asn Gly Leu Thr Ala Trp Asp Lys  
1 5 10 15  
Pro Lys His Cys Pro Asp Arg Glu His Asp Trp Lys Leu Val Gly Met  
20 25 30  
Ser Glu Ala Cys Leu His Arg Lys Ser His Ser Glu Arg Arg Ser Thr  
35 40 45  
Leu Lys Asn Glu Gln Ser Ser Pro His Leu Ile Gln Thr Thr Trp Thr  
50 55 60  
Ser Ser Ile Phe His Leu Asp His Asp Asp Val Asn Asp Gln Ser Val  
65 70 75 80  
Ser Ser Ala Gln Thr Phe Gln Thr Glu Glu Lys Lys Cys Lys Gly Tyr  
85 90 95  
Ile Pro Ser Tyr Leu Asp Lys Asp Glu Leu Cys Val Val Cys Gly Asp  
100 105 110  
Lys Ala Thr Gly Tyr His Tyr Arg Cys Ile Thr Cys Glu Gly Cys Lys  
115 120 125  
Gly Phe Phe Arg Arg Thr Ile Gln Lys Asn Leu His Pro Ser Tyr Ser  
130 135 140  
Cys Lys Tyr Glu Gly Lys Cys Val Ile Asp Lys Val Thr Arg Asn Gln  
145 150 155 160  
Cys Gln Glu Cys Arg Phe Lys Lys Cys Ile Tyr Val Gly Met Ala Thr  
165 170 175  
Asp Leu Val Leu Asp Asp Ser Lys Arg Leu Ala Lys Arg Lys Leu Ile  
180 185 190  
Glu Glu Asn Arg Glu Lys Arg Arg Arg Glu Glu Leu Gln Lys Ser Ile  
195 200 205  
Gly His Lys Pro Glu Pro Thr Asp Glu Glu Trp Glu Leu Ile Lys Thr  
210 215 220  
Val Thr Glu Ala His Val Ala Thr Asn Ala Gln Gly Ser His Trp Lys  
225 230 235 240  
Gln Lys Pro Lys Phe Leu Pro Glu Asp Ile Gly Gln Ala Pro Ile Val  
245 250 255  
Asn Ala Pro Glu Gly Gly Lys Val Asp Leu Glu Ala Phe Ser His Phe  
260 265 270  
Thr Lys Ile Ile Thr Pro Ala Ile Thr Arg Val Val Asp Phe Ala Lys

275

280

285

Lys Leu Pro Met Phe Cys Glu Leu Pro Cys Glu Asp Gln Ile Ile Leu  
290 295 300

Leu Lys Gly Cys Cys Met Glu Ile Met Ser Leu Arg Ala Ala Val Arg  
305 310 315 320

Tyr Asp Pro Glu Ser Glu Thr Leu Thr Leu Asn Gly Glu Met Ala Val  
325 330 335

Ile Arg Gly Gln Leu Lys Asn Gly Gly Leu Gly Val Val Ser Asp Ala  
340 345 350

Ile Phe Asp Leu Gly Met Ser Leu Ser Ser Phe Asn Leu Asp Asp Thr  
355 360 365

Glu Val Ala Leu Leu Gln Ala Val Leu Leu Met Ser Ser Asp Arg Pro  
370 375 380

Gly Leu Ala Cys Val Glu Arg Ile Glu Lys Tyr Gln Asp Ser Phe Leu  
385 390 395 400

Leu Ala Phe Glu His Tyr Ile Asn Tyr Arg Lys His His Val Thr His  
405 410 415

Phe Trp Pro Lys Leu Leu Met Lys Val Thr Asp Leu Arg Met Ile Gly  
420 425 430

Ala Cys His Ala Ser Arg Phe Leu His Met Lys Val Glu Cys Pro Thr  
435 440 445

Glu Leu Leu Pro Pro Leu Phe Leu Glu Val Phe Glu Asp  
450 455 460

&lt;210&gt; 4

&lt;211&gt; 416

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; DOMAIN

&lt;222&gt; (131)..(373)

&lt;223&gt; minimal ligand binding domain

&lt;400&gt; 4

Pro Asn Ser Asn His Val Ala Ser Gly Ala Gly Glu Ala Ala Ile Glu  
1 5 10 15

Thr Gln Ser Ser Ser Ser Glu Glu Ile Val Pro Ser Pro Pro Ser Pro  
20 25 30

Pro Pro Leu Pro Arg Ile Tyr Lys Pro Cys Phe Val Cys Gln Asp Lys  
35 40 45

Ser Ser Gly Tyr His Tyr Gly Val Ser Ala Cys Glu Gly Cys Lys Gly  
 50 55 60  
 Phe Phe Arg Arg Ser Ile Gln Lys Asn Met Val Tyr Thr Cys His Arg  
 65 70 75 80  
 Asp Lys Asn Cys Ile Ile Asn Lys Val Thr Arg Asn Arg Cys Gln Tyr  
 85 90 95  
 Cys Arg Leu Gln Lys Cys Phe Glu Val Gly Met Ser Lys Glu Ser Val  
 100 105 110  
 Arg Asn Asp Arg Asn Lys Lys Lys Lys Glu Val Pro Lys Pro Glu Cys  
 115 120 125  
 Ser Glu Ser Tyr Thr Leu Thr Pro Glu Val Gly Glu Leu Ile Glu Lys  
 130 135 140  
 Val Arg Lys Ala His Gln Glu Thr Phe Pro Ala Leu Cys Gln Leu Gly  
 145 150 155 160  
 Lys Tyr Thr Thr Asn Asn Ser Ser Glu Gln Arg Val Ser Leu Asp Ile  
 165 170 175  
 Asp Leu Trp Asp Lys Phe Ser Glu Leu Ser Thr Lys Cys Ile Ile Lys  
 180 185 190  
 Thr Val Glu Phe Ala Lys Gln Leu Pro Gly Phe Thr Thr Leu Thr Ile  
 195 200 205  
 Ala Asp Gln Ile Thr Leu Leu Lys Ala Ala Cys Leu Asp Ile Leu Ile  
 210 215 220  
 Leu Arg Ile Cys Thr Arg Tyr Thr Pro Glu Gln Asp Thr Met Thr Phe  
 225 230 235 240  
 Ser Asp Gly Leu Thr Leu Asn Arg Thr Gln Met His Asn Ala Gly Phe  
 245 250 255  
 Gly Pro Leu Thr Asp Leu Val Phe Ala Phe Ala Asn Gln Leu Leu Pro  
 260 265 270  
 Leu Glu Met Asp Asp Ala Glu Thr Gly Ile Leu Ser Ala Ile Cys Leu  
 275 280 285  
 Ile Cys Gly Asp Arg Gln Asp Leu Glu Gln Pro Asp Arg Val Asp Met  
 290 295 300  
 Leu Gln Glu Pro Leu Leu Glu Ala Leu Lys Val Tyr Val Arg Lys Arg  
 305 310 315 320  
 Arg Pro Ser Arg Pro His Met Phe Pro Lys Met Leu Met Lys Ile Thr  
 325 330 335  
 Asp Leu Arg Ser Ile Ser Ala Lys Gly Ala Glu Arg Val Ile Thr Leu  
 340 345 350

Lys Met Glu Ile Pro Gly Ser Met Pro Pro Leu Ile Gln Glu Met Leu  
 355 360 365

Glu Asn Ser Glu Gly Leu Asp Thr Leu Ser Gly Gln Pro Gly Gly Gly  
 370 375 380

Gly Arg Asp Gly Gly Gly Leu Ala Pro Pro Pro Gly Ser Cys Ser Pro  
 385 390 395 400

Ser Leu Ser Pro Ser Ser Asn Arg Ser Ser Pro Ala Thr His Ser Pro  
 405 410 415

<210> 5  
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 <212> PRT  
 <213> Homo sapiens

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 <222> (179)..(421)  
 <223> minimal ligand binding domain

<400> 5

Met Ala Thr Asn Lys Glu Arg Leu Phe Ala Ala Gly Ala Leu Gly Pro  
 1 5 10 15

Gly Ser Gly Tyr Pro Gly Ala Gly Phe Pro Phe Ala Phe Pro Gly Ala  
 20 25 30

Leu Arg Gly Ser Pro Pro Phe Glu Met Leu Ser Pro Ser Phe Arg Gly  
 35 40 45

Leu Gly Gln Pro Asp Leu Pro Lys Glu Met Ala Ser Leu Ser Val Glu  
 50 55 60

Thr Gln Ser Thr Ser Ser Glu Glu Met Val Pro Ser Ser Pro Ser Pro  
 65 70 75 80

Pro Pro Pro Pro Arg Val Tyr Lys Pro Cys Phe Val Cys Asn Asp Lys  
 85 90 95

Ser Ser Gly Tyr His Tyr Gly Val Ser Ser Cys Glu Gly Cys Lys Gly  
 100 105 110

Phe Phe Arg Arg Ser Ile Gln Lys Asn Met Val Tyr Thr Cys His Arg  
 115 120 125

Asp Lys Asn Cys Ile Ile Asn Lys Val Thr Arg Asn Arg Cys Gln Tyr  
 130 135 140

Cys Arg Leu Gln Lys Cys Phe Glu Val Gly Met Ser Lys Glu Ala Val  
 145 150 155 160

Arg Asn Asp Arg Asn Lys Lys Lys Lys Glu Val Lys Glu Glu Gly Ser  
 165 170 175





<212> PRT  
 <213> Homo sapiens

<220>  
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 <222> (231)..(460)  
 <223> minimal ligand binding domain

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Met Asp Thr Lys His Phe Leu Pro Leu Asp Phe Ser Thr Gln Val Asn  
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 20 25 30  
 Leu His Pro Ser Leu Gly Pro Gly Ile Gly Ser Pro Gly Gln Leu His  
 35 40 45  
 Ser Pro Ile Ser Thr Leu Ser Ser Pro Ile Asn Gly Met Gly Pro Pro  
 50 55 60  
 Phe Ser Val Ile Ser Ser Pro Met Gly Pro His Ser Met Ser Val Pro  
 65 70 75 80  
 Thr Thr Pro Thr Leu Gly Phe Ser Thr Gly Ser Pro Gln Leu Ser Ser  
 85 90 95  
 Pro Met Asn Pro Val Ser Ser Ser Glu Asp Ile Lys Pro Pro Leu Gly  
 100 105 110  
 Leu Asn Gly Val Leu Lys Val Pro Ala His Pro Ser Gly Asn Met Ala  
 115 120 125  
 Ser Phe Thr Lys His Ile Cys Ala Ile Cys Gly Asp Arg Ser Ser Gly  
 130 135 140  
 Lys His Tyr Gly Val Tyr Ser Cys Glu Gly Cys Lys Gly Phe Phe Lys  
 145 150 155 160  
 Arg Thr Val Arg Lys Asp Leu Thr Tyr Thr Cys Arg Asp Asn Lys Asp  
 165 170 175  
 Cys Leu Ile Asp Lys Arg Gln Arg Asn Arg Cys Gln Tyr Cys Arg Tyr  
 180 185 190  
 Gln Lys Cys Leu Ala Met Gly Met Lys Arg Glu Ala Val Gln Glu Glu  
 195 200 205  
 Arg Gln Arg Gly Lys Asp Arg Asn Glu Asn Glu Val Glu Ser Thr Ser  
 210 215 220  
 Ser Ala Asn Glu Asp Met Pro Val Glu Arg Ile Leu Glu Ala Glu Leu  
 225 230 235 240  
 Ala Val Glu Pro Lys Thr Glu Thr Tyr Val Glu Ala Asn Met Gly Leu

245							250					255				
Asn	Pro	Ser	Ser	Pro	Asn	Asp	Pro	Val	Thr	Asn	Ile	Cys	Gln	Ala	Ala	
			260					265					270			
Asp	Lys	Gln	Leu	Phe	Thr	Leu	Val	Glu	Trp	Ala	Lys	Arg	Ile	Pro	His	
		275					280					285				
Phe	Ser	Glu	Leu	Pro	Leu	Asp	Asp	Gln	Val	Ile	Leu	Leu	Arg	Ala	Gly	
	290					295					300					
Trp	Asn	Glu	Leu	Leu	Ile	Ala	Ser	Phe	Ser	His	Arg	Ser	Ile	Ala	Val	
305					310					315					320	
Lys	Asp	Gly	Ile	Leu	Leu	Ala	Thr	Gly	Leu	His	Val	His	Arg	Asn	Ser	
				325					330					335		
Ala	His	Ser	Ala	Gly	Val	Gly	Ala	Ile	Phe	Asp	Arg	Val	Leu	Thr	Glu	
			340					345					350			
Leu	Val	Ser	Lys	Met	Arg	Asp	Met	Gln	Met	Asp	Lys	Thr	Glu	Leu	Gly	
		355					360					365				
Cys	Leu	Arg	Ala	Ile	Val	Leu	Phe	Asn	Pro	Asp	Ser	Lys	Gly	Leu	Ser	
	370					375					380					
Asn	Pro	Ala	Glu	Val	Glu	Ala	Leu	Arg	Glu	Lys	Val	Tyr	Ala	Ser	Leu	
385					390					395					400	
Glu	Ala	Tyr	Cys	Lys	His	Lys	Tyr	Pro	Glu	Gln	Pro	Gly	Arg	Phe	Ala	
				405					410					415		
Lys	Leu	Leu	Leu	Arg	Leu	Pro	Ala	Leu	Arg	Ser	Ile	Gly	Leu	Lys	Cys	
			420					425					430			
Leu	Glu	His	Leu	Phe	Phe	Phe	Lys	Leu	Ile	Gly	Asp	Thr	Pro	Ile	Asp	
		435					440					445				
Thr	Phe	Leu	Met	Glu	Met	Leu	Glu	Ala	Pro	His	Gln	Met	Thr			
	450					455					460					

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<210> 7
<211> 525
<212> PRT
<213> Homo sapiens
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<400> 7

Gly	Ser	Val	Gly	Arg	Trp	Gly	Ala	Lys	Glu	Cys	Ile	Val	Gly	Ser	Ala
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Thr	Ala	Leu	Ala	Gly	Ser	Arg	Ser	Gly	Gly	Gly	Gly	Gly	Gly	Gly	Arg
		35					40					45			
Arg	Arg	Thr	Thr	Asn	Pro	Gly	Ala	Gly	Ala	Arg	Gly	Trp	Thr	Gly	Arg
	50					55					60				
Asp	Gly	Arg	His	Gly	Arg	Asp	Ser	Arg	Ser	Pro	Asp	Ser	Ser	Ser	Pro
65					70					75					80
Asn	Pro	Leu	Pro	Gln	Gly	Val	Pro	Pro	Pro	Ser	Pro	Pro	Gly	Pro	Pro
				85					90					95	
Leu	Pro	Pro	Ser	Thr	Ala	Pro	Thr	Leu	Gly	Gly	Ser	Gly	Ala	Pro	Pro
			100					105					110		
Pro	Pro	Pro	Met	Pro	Pro	Pro	Pro	Leu	Gly	Ser	Pro	Phe	Pro	Val	Ile
		115					120					125			
Ser	Ser	Ser	Met	Gly	Ser	Pro	Gly	Leu	Pro	Pro	Pro	Ala	Pro	Pro	Gly
	130					135					140				
Phe	Ser	Gly	Pro	Val	Ser	Ser	Pro	Gln	Ile	Asn	Ser	Thr	Val	Ser	Leu
145					150					155					160
Pro	Gly	Gly	Gly	Ser	Gly	Pro	Pro	Glu	Asp	Val	Lys	Pro	Pro	Val	Leu
				165					170					175	
Gly	Val	Arg	Gly	Leu	His	Cys	Pro	Pro	Pro	Pro	Gly	Gly	Pro	Gly	Ala
			180					185					190		
Gly	Lys	Arg	Leu	Cys	Ala	Ile	Cys	Gly	Asp	Arg	Ser	Ser	Gly	Lys	His
		195					200					205			
Tyr	Gly	Val	Tyr	Ser	Cys	Glu	Gly	Cys	Lys	Gly	Phe	Phe	Lys	Arg	Thr
	210					215					220				
Ile	Arg	Lys	Asp	Leu	Thr	Tyr	Ser	Cys	Arg	Asp	Asn	Lys	Asp	Cys	Thr
225					230					235					240
Val	Asp	Lys	Arg	Gln	Arg	Asn	Arg	Cys	Gln	Tyr	Cys	Arg	Tyr	Gln	Lys
				245					250					255	
Cys	Leu	Ala	Thr	Gly	Met	Lys	Arg	Glu	Ala	Val	Gln	Glu	Glu	Arg	Gln
			260					265					270		
Arg	Gly	Lys	Asp	Lys	Asp	Gly	Asp	Gly	Glu	Cys	Ala	Gly	Gly	Ala	Pro
		275					280					285			
Glu	Glu	Met	Pro	Val	Asp	Arg	Ile	Leu	Glu	Ala	Glu	Leu	Ala	Val	Glu
	290					295					300				
Gln	Lys	Ser	Asp	Gln	Gly	Val	Glu	Gly	Pro	Gly	Gly	Thr	Gly	Gly	Ser
305					310					315					320

Gly	Ser	Ser	Pro	Asn	Asp	Pro	Val	Thr	Asn	Ile	Cys	Gln	Ala	Ala	Asp	
				325					330						335	
Lys	Gln	Leu	Phe	Thr	Leu	Val	Glu	Trp	Ala	Lys	Arg	Ile	Pro	His	Phe	
			340					345					350			
Ser	Ser	Leu	Pro	Leu	Asp	Asp	Gln	Val	Ile	Leu	Leu	Arg	Ala	Gly	Trp	
		355					360					365				
Asn	Glu	Leu	Leu	Ile	Ala	Ser	Phe	Ser	His	Arg	Ser	Ile	Asp	Val	Arg	
	370					375					380					
Asp	Gly	Ile	Leu	Leu	Ala	Thr	Gly	Leu	His	Val	His	Arg	Asn	Ser	Ala	
385					390					395						400
His	Ser	Ala	Gly	Val	Gly	Ala	Ile	Phe	Asp	Arg	Val	Leu	Thr	Glu	Leu	
			405					410						415		
Val	Ser	Lys	Met	Arg	Asp	Met	Arg	Met	Asp	Lys	Thr	Glu	Leu	Gly	Cys	
			420					425					430			
Leu	Arg	Ala	Ile	Ile	Leu	Phe	Asn	Pro	Asp	Ala	Lys	Gly	Leu	Ser	Asn	
		435					440					445				
Pro	Ser	Glu	Val	Glu	Val	Leu	Arg	Glu	Lys	Val	Tyr	Ala	Ser	Leu	Glu	
	450					455					460					
Thr	Tyr	Cys	Lys	Gln	Lys	Tyr	Pro	Glu	Gln	Gln	Gly	Arg	Phe	Ala	Lys	
465					470					475					480	
Leu	Leu	Leu	Arg	Leu	Pro	Ala	Leu	Arg	Ser	Ile	Gly	Leu	Lys	Cys	Leu	
			485						490					495		
Glu	His	Leu	Phe	Phe	Phe	Lys	Leu	Ile	Gly	Asp	Thr	Pro	Ile	Asp	Thr	
			500					505					510			
Phe	Leu	Met	Glu	Met	Leu	Glu	Ala	Pro	His	Gln	Leu	Ala				
		515					520					525				

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<210>      8
<211>      468
<212>      PRT
<213>      Homo sapiens

<220>
<221>      DOMAIN
<222>      (196)..(468)
<223>      minimal ligand binding domain
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Met Val Asp Thr Glu Ser Pro Leu Cys Pro Leu Ser Pro Leu Glu Ala  
1 5 10 15

Asn	Ile	Gln	Glu	Ile	Ser	Gln	Ser	Ile	Gly	Glu	Asp	Ser	Ser	Gly	Ser	
		35					40					45				
Phe	Gly	Phe	Thr	Glu	Tyr	Gln	Tyr	Leu	Gly	Ser	Cys	Pro	Gly	Ser	Asp	
	50					55					60					
Gly	Ser	Val	Ile	Thr	Asp	Thr	Leu	Ser	Pro	Ala	Ser	Ser	Pro	Ser	Ser	
65					70					75					80	
Val	Thr	Tyr	Pro	Val	Val	Pro	Gly	Ser	Val	Asp	Glu	Ser	Pro	Ser	Gly	
				85					90					95		
Ala	Leu	Asn	Ile	Glu	Cys	Arg	Ile	Cys	Gly	Asp	Lys	Ala	Ser	Gly	Tyr	
			100					105						110		
His	Tyr	Gly	Val	His	Ala	Cys	Glu	Gly	Cys	Lys	Gly	Phe	Phe	Arg	Arg	
		115					120					125				
Thr	Ile	Arg	Leu	Lys	Leu	Val	Tyr	Asp	Lys	Cys	Asp	Arg	Ser	Cys	Lys	
	130					135					140					
Ile	Gln	Lys	Lys	Asn	Arg	Asn	Lys	Cys	Gln	Tyr	Cys	Arg	Phe	His	Lys	
145					150					155					160	
Cys	Leu	Ser	Val	Gly	Met	Ser	His	Asn	Ala	Ile	Arg	Phe	Gly	Arg	Met	
				165					170					175		
Pro	Arg	Ser	Glu	Lys	Ala	Lys	Leu	Lys	Ala	Glu	Ile	Leu	Thr	Cys	Glu	
			180					185						190		
His	Asp	Ile	Glu	Asp	Ser	Glu	Thr	Ala	Asp	Leu	Lys	Ser	Leu	Ala	Lys	
		195					200					205				
Arg	Ile	Tyr	Glu	Ala	Tyr	Leu	Lys	Asn	Phe	Asn	Met	Asn	Lys	Val	Lys	
	210					215					220					
Ala	Arg	Val	Ile	Leu	Ser	Gly	Lys	Ala	Ser	Asn	Asn	Pro	Pro	Phe	Val	
225					230					235					240	
Ile	His	Asp	Met	Glu	Thr	Leu	Cys	Met	Ala	Glu	Lys	Thr	Leu	Val	Ala	
				245					250					255		
Lys	Leu	Val	Ala	Asn	Gly	Ile	Gln	Asn	Lys	Glu	Val	Glu	Val	Arg	Ile	
			260					265						270		
Phe	His	Cys	Cys	Gln	Cys	Thr	Ser	Val	Glu	Thr	Val	Thr	Glu	Leu	Thr	
		275					280					285				
Glu	Phe	Ala	Lys	Ala	Ile	Pro	Ala	Phe	Ala	Asn	Leu	Asp	Leu	Asn	Asp	
	290					295					300					
Gln	Val	Thr	Leu	Leu	Lys	Tyr	Gly	Val	Tyr	Glu	Ala	Ile	Phe	Ala	Met	
305					310					315					320	
Leu	Ser	Ser	Val	Met	Asn	Lys	Asp	Gly	Met	Leu	Val	Ala	Tyr	Gly	Asn	
				325					330					335		

Gly Phe Ile Thr Arg Glu Phe Leu Lys Ser Leu Arg Lys Pro Phe Cys  
 340 345 350

Asp Ile Met Glu Pro Lys Phe Asp Phe Ala Met Lys Phe Asn Ala Leu  
 355 360 365

Glu Leu Asp Asp Ser Asp Ile Ser Leu Phe Val Ala Ala Ile Ile Cys  
 370 375 380

Cys Gly Asp Arg Pro Gly Leu Leu Asn Val Gly His Ile Glu Lys Met  
 385 390 395 400

Gln Glu Gly Ile Val His Val Leu Arg Leu His Leu Gln Ser Asn His  
 405 410 415

Pro Asp Asp Ile Phe Leu Phe Pro Lys Leu Leu Gln Lys Met Ala Asp  
 420 425 430

Leu Arg Gln Leu Val Thr Glu His Ala Gln Leu Val Gln Ile Ile Lys  
 435 440 445

Lys Thr Glu Ser Asp Ala Ala Leu His Pro Leu Leu Gln Glu Ile Tyr  
 450 455 460

Arg Asp Met Tyr  
 465

<210> 9  
 <211> 441  
 <212> PRT  
 <213> Homo sapiens

<220>  
 <221> DOMAIN  
 <222> (168)..(441)  
 <223> minimal ligand binding domain

<400> 9

Met Glu Gln Pro Gln Glu Glu Ala Pro Glu Val Arg Glu Glu Glu Glu  
 1 5 10 15

Lys Glu Glu Val Ala Glu Ala Glu Gly Ala Pro Glu Leu Asn Gly Gly  
 20 25 30

Pro Gln His Ala Leu Pro Ser Ser Ser Tyr Thr Asp Leu Ser Arg Ser  
 35 40 45

Ser Ser Pro Pro Ser Leu Leu Asp Gln Leu Gln Met Gly Cys Asp Gly  
 50 55 60

Ala Ser Cys Gly Ser Leu Asn Met Glu Cys Arg Val Cys Gly Asp Lys  
 65 70 75 80

Ala Ser Gly Phe His Tyr Gly Val His Ala Cys Glu Gly Cys Lys Gly

85								90				95			
Phe	Phe	Arg	Arg	Thr	Ile	Arg	Met	Lys	Leu	Glu	Tyr	Glu	Lys	Cys	Glu
			100					105					110		
Arg	Ser	Cys	Lys	Ile	Gln	Lys	Lys	Asn	Arg	Asn	Lys	Cys	Gln	Tyr	Cys
		115					120					125			
Arg	Phe	Gln	Lys	Cys	Leu	Ala	Leu	Gly	Met	Ser	His	Asn	Ala	Ile	Arg
	130					135					140				
Phe	Gly	Arg	Met	Pro	Glu	Ala	Glu	Lys	Arg	Lys	Leu	Val	Ala	Gly	Leu
145					150					155					160
Thr	Ala	Asn	Glu	Gly	Ser	Gln	Tyr	Asn	Pro	Gln	Val	Ala	Asp	Leu	Lys
				165					170					175	
Ala	Phe	Ser	Lys	His	Ile	Tyr	Asn	Ala	Tyr	Leu	Lys	Asn	Phe	Asn	Met
			180					185					190		
Thr	Lys	Lys	Lys	Ala	Arg	Ser	Ile	Leu	Thr	Gly	Lys	Ala	Ser	His	Thr
		195					200					205			
Ala	Pro	Phe	Val	Ile	His	Asp	Ile	Glu	Thr	Leu	Trp	Gln	Ala	Glu	Lys
	210					215					220				
Gly	Leu	Val	Trp	Lys	Gln	Leu	Val	Asn	Gly	Leu	Pro	Pro	Tyr	Lys	Glu
225					230					235					240
Ile	Ser	Val	His	Val	Phe	Tyr	Arg	Cys	Gln	Cys	Thr	Thr	Val	Glu	Thr
				245					250					255	
Val	Arg	Glu	Leu	Thr	Glu	Phe	Ala	Lys	Ser	Ile	Pro	Ser	Phe	Ser	Ser
			260					265					270		
Leu	Phe	Leu	Asn	Asp	Gln	Val	Thr	Leu	Leu	Lys	Tyr	Gly	Val	His	Glu
		275					280					285			
Ala	Ile	Phe	Ala	Met	Leu	Ala	Ser	Ile	Val	Asn	Lys	Asp	Gly	Leu	Leu
	290					295					300				
Val	Ala	Asn	Gly	Ser	Gly	Phe	Val	Thr	Arg	Glu	Phe	Leu	Arg	Ser	Leu
305					310					315					320
Arg	Lys	Pro	Phe	Ser	Asp	Ile	Ile	Glu	Pro	Lys	Phe	Glu	Phe	Ala	Val
				325					330					335	
Lys	Phe	Asn	Ala	Leu	Glu	Leu	Asp	Asp	Ser	Asp	Leu	Ala	Leu	Phe	Ile
			340					345					350		
Ala	Ala	Ile	Ile	Leu	Cys	Gly	Asp	Arg	Pro	Gly	Leu	Met	Asn	Val	Pro
		355					360					365			
Arg	Val	Glu	Ala	Ile	Gln	Asp	Thr	Ile	Leu	Arg	Ala	Leu	Glu	Phe	His
	370					375					380				
Leu	Gln	Ala	Asn	His	Pro	Asp	Ala	Gln	Tyr	Leu	Phe	Pro	Lys	Leu	Leu



385                      390                      395                      400

Gln Lys Met Ala Asp Leu Arg Gln Leu Val Thr Glu His Ala Gln Met  
                                  405                                   410                                   415

Met Gln Arg Ile Lys Lys Thr Glu Thr Glu Thr Ser Leu His Pro Leu  
                                  420                                   425                                   430

Leu Gln Glu Ile Tyr Lys Asp Met Tyr  
                                  435                                   440

<210> 10  
 <211> 475  
 <212> PRT  
 <213> Homo sapiens

<220>  
 <221> DOMAIN  
 <222> (202)..(475)  
 <223> minimal ligand binding domain

<400> 10

Met Val Asp Thr Glu Met Pro Phe Trp Pro Thr Asn Phe Gly Ile Ser  
 1                                   5                                   10                                   15

Ser Val Asp Leu Ser Met Met Asp Asp His Ser His Ser Phe Asp Ile  
                                  20                                   25                                   30

Lys Pro Phe Thr Thr Val Asp Phe Ser Ser Ile Ser Ala Pro His Tyr  
                                  35                                   40                                   45

Glu Asp Ile Pro Phe Thr Arg Ala Asp Pro Met Val Ala Asp Tyr Lys  
                                  50                                   55                                   60

Tyr Asp Leu Lys Leu Gln Glu Tyr Gln Ser Ala Ile Lys Val Glu Pro  
 65                                   70                                   75                                   80

Ala Ser Pro Pro Tyr Tyr Ser Glu Lys Ala Gln Leu Tyr Asn Arg Pro  
                                  85                                   90                                   95

His Glu Glu Pro Ser Asn Ser Leu Met Ala Ile Glu Cys Arg Val Cys  
                                  100                                   105                                   110

Gly Asp Lys Ala Ser Gly Phe His Tyr Gly Val His Ala Cys Glu Gly  
                                  115                                   120                                   125

Cys Lys Gly Phe Phe Arg Arg Thr Ile Arg Leu Lys Leu Ile Tyr Asp  
                                  130                                   135                                   140

Arg Cys Asp Leu Asn Cys Arg Ile His Lys Lys Ser Arg Asn Lys Cys  
 145                                   150                                   155                                   160

Gln Tyr Cys Arg Phe Gln Lys Cys Leu Ala Val Gly Met Ser His Asn  
                                  165                                   170                                   175

Ala Ile Arg Phe Gly Arg Met Pro Gln Ala Glu Lys Glu Lys Leu Leu  
 180 185 190  
 Ala Glu Ile Ser Ser Asp Ile Asp Gln Leu Asn Pro Glu Ser Ala Asp  
 195 200 205  
 Leu Arg Ala Leu Ala Lys His Leu Tyr Asp Ser Tyr Ile Lys Ser Phe  
 210 215 220  
 Pro Leu Thr Lys Ala Lys Ala Arg Ala Ile Leu Thr Gly Lys Thr Thr  
 225 230 235 240  
 Asp Lys Ser Pro Phe Val Ile Tyr Asp Met Asn Ser Leu Met Met Gly  
 245 250 255  
 Glu Asp Lys Ile Lys Phe Lys His Ile Thr Pro Leu Gln Glu Gln Ser  
 260 265 270  
 Lys Glu Val Ala Ile Arg Ile Phe Gln Gly Cys Gln Phe Arg Ser Val  
 275 280 285  
 Glu Ala Val Gln Glu Ile Thr Glu Tyr Ala Lys Asn Ile Pro Gly Phe  
 290 295 300  
 Ile Asn Leu Asp Leu Asn Asp Gln Val Thr Leu Leu Lys Tyr Gly Val  
 305 310 315 320  
 His Glu Ile Ile Tyr Thr Met Leu Ala Ser Leu Met Asn Lys Asp Gly  
 325 330 335  
 Val Leu Ile Ser Glu Gly Gln Gly Phe Met Thr Arg Glu Phe Leu Lys  
 340 345 350  
 Ser Leu Arg Lys Pro Phe Gly Asp Phe Met Glu Pro Lys Phe Glu Phe  
 355 360 365  
 Ala Val Lys Phe Asn Ala Leu Glu Leu Asp Asp Ser Asp Leu Ala Ile  
 370 375 380  
 Phe Ile Ala Val Ile Ile Leu Ser Gly Asp Arg Pro Gly Leu Leu Asn  
 385 390 395 400  
 Val Lys Pro Ile Glu Asp Ile Gln Asp Asn Leu Leu Gln Ala Leu Glu  
 405 410 415  
 Leu Gln Leu Lys Leu Asn His Pro Glu Ser Ser Gln Leu Phe Ala Lys  
 420 425 430  
 Val Leu Gln Lys Met Thr Asp Leu Arg Gln Ile Val Thr Glu His Val  
 435 440 445  
 Gln Leu Leu His Val Ile Lys Lys Thr Glu Thr Asp Met Ser Leu His  
 450 455 460  
 Pro Leu Leu Gln Glu Ile Tyr Lys Asp Leu Tyr  
 465 470 475

<210> 11  
 <211> 609  
 <212> PRT  
 <213> Homo sapiens

<220>  
 <221> DOMAIN  
 <222> (295)..(585)  
 <223> minimal ligand binding domain

<400> 11

Met Asp Thr Glu Asp Leu Pro Ala Asn Asn Ala Pro Leu Thr Val Asn  
 1 5 10 15  
 Glu Gln Leu Leu Gly Ser Cys Thr Leu Lys Phe Pro Ala Gln Asp Ala  
 20 25 30  
 Gln Val Ile Val Met Ser Gly Gln Glu Thr Ile Arg Val Leu Glu Val  
 35 40 45  
 Glu Val Asp Thr Ala Leu Ser Ser Ala Gly Ala Ala Glu Ser Gly Gly  
 50 55 60  
 Asp Glu Glu Gly Ser Gly Gln Ser Leu Glu Ala Thr Glu Glu Ala Gln  
 65 70 75 80  
 Leu Asp Gly Pro Val Thr Thr Ser Ser Thr Thr Ala Val Thr Val Glu  
 85 90 95  
 Val Ser Ala Pro Val Val Gln Thr Val Val Ser Lys Ala Ala Ile Ser  
 100 105 110  
 Val Ser Pro Ala Gln Gln Thr Ser Val Pro Ile Thr Val Gln Ala Cys  
 115 120 125  
 Pro Gln Val Leu Thr Gln Asp Gly Leu Ala Ser Leu Met Thr Gly Met  
 130 135 140  
 Leu Ala Gln Gln Ser Ser Leu Gly Gln Pro Leu Leu Ile Pro Leu Ser  
 145 150 155 160  
 Met Ala Gly Ser Val Gly Gly Gln Gly Gly Leu Ala Val Leu Thr Leu  
 165 170 175  
 Pro Thr Ala Thr Val Ala Thr Leu Pro Gly Leu Ala Ala Ala Ser Pro  
 180 185 190  
 Ala Gly Gly Leu Leu Lys Leu Pro Phe Ala Gly Leu Gln Ala Ala Thr  
 195 200 205  
 Val Leu Asn Ser Val Gln Thr Gln Leu Gln Ala Pro Ala Gln Ala Val  
 210 215 220  
 Leu Gln Pro Gln Met Ser Ala Leu Ala Met Gln Gln Thr Gln Thr Thr  
 225 230 235 240

Ala Ala Thr Thr Ala Ser Ile Val Gln Lys Ala Ser Glu Pro Ser Val  
 245 250 255  
 Ser Val Ala Thr Leu Gln Thr Ala Gly Leu Ser Ile Asn Pro Ala Ile  
 260 265 270  
 Ile Ser Ala Ala Ser Leu Gly Ala Gln Pro Gln Phe Ile Ser Ser Leu  
 275 280 285  
 Thr Thr Thr Pro Ile Ile Thr Ser Ala Met Ser Asn Val Ala Gly Leu  
 290 295 300  
 Thr Ser Gln Leu Ile Thr Asn Ala Gln Gly Gln Val Ile Gly Thr Leu  
 305 310 315 320  
 Pro Leu Leu Val Asn Pro Ala Ser Leu Ala Gly Ala Ala Ala Ala Ser  
 325 330 335  
 Ala Leu Pro Ala Gln Gly Leu Gln Val Gln Thr Val Ala Pro Gln Leu  
 340 345 350  
 Leu Leu Asn Ser Gln Gly Gln Ile Ile Ala Thr Ile Gly Asn Gly Pro  
 355 360 365  
 Thr Ala Ala Ile Pro Ser Thr Ala Ser Val Leu Pro Lys Ala Thr Val  
 370 375 380  
 Pro Leu Thr Leu Thr Lys Thr Thr Thr Gln Gly Pro Val Gly Lys Val  
 385 390 395 400  
 Ala Pro Ser Lys Val Ile Ile Ala Pro Gln Pro Ser Val Val Lys Pro  
 405 410 415  
 Val Thr Ser Leu Thr Ala Ala Gly Val Ile Ala Cys Gly Glu Met Pro  
 420 425 430  
 Thr Val Gly Gln Leu Val Asn Lys Pro Ser Ala Val Lys Asp Glu Glu  
 435 440 445  
 Ala Ile Asn Leu Glu Glu Ile Arg Glu Phe Ala Lys Asn Phe Lys Ile  
 450 455 460  
 Arg Arg Leu Ser Leu Gly Leu Thr Gln Thr Gln Val Gly Gln Ala Leu  
 465 470 475 480  
 Thr Ala Thr Glu Gly Pro Ala Tyr Ser Gln Ser Ala Ile Cys Arg Phe  
 485 490 495  
 Glu Lys Leu Asp Ile Thr Pro Lys Ser Ala Gln Lys Leu Lys Pro Val  
 500 505 510  
 Leu Glu Arg Trp Leu Ala Glu Ala Glu Leu Trp Asn Gln Lys Gly Gln  
 515 520 525  
 Gln Asn Leu Met Glu Phe Val Gly Gly Glu Pro Ser Lys Lys Arg Lys  
 530 535 540

Arg Arg Thr Ser Phe Thr Pro Gln Ala Ile Glu Val Leu Asn Thr Tyr  
545 550 555 560

Phe Glu Lys Asn Ser Leu Pro Thr Gly Gln Glu Ile Thr Glu Ile Ala  
565 570 575

Lys Glu Leu Asn Tyr Asp Arg Glu Val Val Arg Val Trp Phe Cys Asn  
580 585 590

Arg Arg Gln Thr Leu Lys Asn Thr Ser Lys Ile Asn Val Phe Gln Ser  
595 600 605

Gln

<210> 12  
<211> 595  
<212> PRT  
<213> Homo sapiens

<220>  
<221> DOMAIN  
<222> (287)..(549)  
<223> minimal ligand binding domain

<400> 12

Met Thr Met Thr Leu His Thr Lys Ala Ser Gly Met Ala Leu Leu His  
1 5 10 15

Gln Ile Gln Gly Asn Glu Leu Glu Pro Leu Asn Arg Pro Gln Leu Lys  
20 25 30

Ile Pro Leu Glu Arg Pro Leu Gly Glu Val Tyr Leu Asp Ser Ser Lys  
35 40 45

Pro Ala Val Tyr Asn Tyr Pro Glu Gly Ala Ala Tyr Glu Phe Asn Ala  
50 55 60

Ala Ala Ala Ala Asn Ala Gln Val Tyr Gly Gln Thr Gly Leu Pro Tyr  
65 70 75 80

Gly Pro Gly Ser Glu Ala Ala Ala Phe Gly Ser Asn Gly Leu Gly Gly  
85 90 95

Phe Pro Pro Leu Asn Ser Val Ser Pro Ser Pro Leu Met Leu Leu His  
100 105 110

Pro Pro Pro Gln Leu Ser Pro Phe Leu Gln Pro His Gly Gln Gln Val  
115 120 125

Pro Tyr Tyr Leu Glu Asn Glu Pro Ser Gly Tyr Thr Val Arg Glu Ala  
130 135 140

Gly Pro Pro Ala Phe Tyr Arg Pro Asn Ser Asp Asn Arg Arg Gln Gly

145		150		155		160
Gly Arg Glu Arg	Leu Ala Ser Thr	Asn Asp Lys Gly Ser Met	Ala Met			
	165	170	175			
Glu Ser Ala Lys	Glu Thr Arg Tyr	Cys Ala Val Cys Asn Asp Tyr Ala				
	180	185	190			
Ser Gly Tyr His	Tyr Gly Val Trp	Ser Cys Glu Gly Cys Lys Ala Phe				
	195	200	205			
Phe Lys Arg Ser	Ile Gln Gly His	Asn Asp Tyr Met Cys Pro Ala Thr				
	210	215	220			
Asn Gln Cys Thr	Ile Asp Lys Asn Arg Arg	Lys Ser Cys Gln Ala Cys				
	225	230	235			240
Arg Leu Arg Lys	Cys Tyr Glu Val Gly	Met Met Lys Gly Gly Ile Arg				
	245	250	255			
Lys Asp Arg Arg	Gly Gly Arg Met	Leu Lys His Lys Arg Gln Arg Asp				
	260	265	270			
Asp Gly Glu Gly	Arg Gly Glu Val Gly	Ser Ala Gly Asp Met Arg Ala				
	275	280	285			
Ala Asn Leu Trp	Pro Ser Pro Leu Met	Ile Lys Arg Ser Lys Lys Asn				
	290	295	300			
Ser Leu Ala Leu	Ser Leu Thr Ala Asp	Gln Met Val Ser Ala Leu Leu				
	305	310	315			320
Asp Ala Glu Pro	Pro Ile Leu Tyr Ser	Glu Tyr Asp Pro Thr Arg Pro				
	325	330	335			
Phe Ser Glu Ala	Ser Met Met Gly	Leu Leu Thr Asn Leu Ala Asp Arg				
	340	345	350			
Glu Leu Val His	Met Ile Asn Trp	Ala Lys Arg Val Pro Gly Phe Val				
	355	360	365			
Asp Leu Thr Leu	His Asp Gln Val His	Leu Leu Glu Cys Ala Trp Leu				
	370	375	380			
Glu Ile Leu Met	Ile Gly Leu Val Trp	Arg Ser Met Glu His Pro Gly				
	385	390	395			400
Lys Leu Leu Phe	Ala Pro Asn Leu Leu	Leu Asp Arg Asn Gln Gly Lys				
	405	410	415			
Cys Val Glu Gly	Met Val Glu Ile Phe	Asp Met Leu Leu Ala Thr Ser				
	420	425	430			
Ser Arg Phe Arg	Met Met Asn Leu Gln	Gly Glu Glu Phe Val Cys Leu				
	435	440	445			
Lys Ser Ile Ile	Leu Leu Asn Ser Gly	Val Tyr Thr Phe Leu Ser Ser				

450

455

460

Thr Leu Lys Ser Leu Glu Glu Lys Asp His Ile His Arg Val Leu Asp  
 465 470 475 480

Lys Ile Thr Asp Thr Leu Ile His Leu Met Ala Lys Ala Gly Leu Thr  
 485 490 495

Leu Gln Gln Gln His Gln Arg Leu Ala Gln Leu Leu Leu Ile Leu Ser  
 500 505 510

His Ile Arg His Met Ser Asn Lys Gly Met Glu His Leu Tyr Ser Met  
 515 520 525

Lys Cys Lys Asn Val Val Pro Leu Tyr Asp Leu Leu Leu Glu Met Leu  
 530 535 540

Asp Ala His Arg Leu His Ala Pro Thr Ser Arg Gly Gly Ala Ser Val  
 545 550 555 560

Glu Glu Thr Asp Gln Ser His Leu Ala Thr Ala Gly Ser Thr Ser Ser  
 565 570 575

His Ser Leu Gln Lys Tyr Tyr Ile Thr Gly Glu Ala Glu Gly Phe Pro  
 580 585 590

Ala Thr Val  
 595

<210> 13

<211> 777

<212> PRT

<213> Homo sapiens

<220>

<221> DOMAIN

<222> (506)..(762)

<223> minimal ligand binding domain

<400> 13

Met Asp Ser Lys Glu Ser Leu Thr Pro Gly Arg Glu Glu Asn Pro Ser  
 1 5 10 15

Ser Val Leu Ala Gln Glu Arg Gly Asp Val Met Asp Phe Tyr Lys Thr  
 20 25 30

Leu Arg Gly Gly Ala Thr Val Lys Val Ser Ala Ser Ser Pro Ser Leu  
 35 40 45

Ala Val Ala Ser Gln Ser Asp Ser Lys Gln Arg Arg Leu Leu Val Asp  
 50 55 60

Phe Pro Lys Gly Ser Val Ser Asn Ala Gln Gln Pro Asp Leu Ser Lys  
 65 70 75 80

Ala Val Ser Leu Ser Met Gly Leu Tyr Met Gly Glu Thr Glu Thr Lys  
 85 90 95  
 Val Met Gly Asn Asp Leu Gly Phe Pro Gln Gln Gly Gln Ile Ser Leu  
 100 105 110  
 Ser Ser Gly Glu Thr Asp Leu Lys Leu Leu Glu Glu Ser Ile Ala Asn  
 115 120 125  
 Leu Asn Arg Ser Thr Ser Val Pro Glu Asn Pro Lys Ser Ser Ala Ser  
 130 135 140  
 Thr Ala Val Ser Ala Ala Pro Thr Glu Lys Glu Phe Pro Lys Thr His  
 145 150 155 160  
 Ser Asp Val Ser Ser Glu Gln Gln His Leu Lys Gly Gln Thr Gly Thr  
 165 170 175  
 Asn Gly Gly Asn Val Lys Leu Tyr Thr Thr Asp Gln Ser Thr Phe Asp  
 180 185 190  
 Ile Leu Gln Asp Leu Glu Phe Ser Ser Gly Ser Pro Gly Lys Glu Thr  
 195 200 205  
 Asn Glu Ser Pro Trp Arg Ser Asp Leu Leu Ile Asp Glu Asn Cys Leu  
 210 215 220  
 Leu Ser Pro Leu Ala Gly Glu Asp Asp Ser Phe Leu Leu Glu Gly Asn  
 225 230 235 240  
 Ser Asn Glu Asp Cys Lys Pro Leu Ile Leu Pro Asp Thr Lys Pro Lys  
 245 250 255  
 Ile Lys Asp Asn Gly Asp Leu Val Leu Ser Ser Pro Ser Asn Val Thr  
 260 265 270  
 Leu Pro Gln Val Lys Thr Glu Lys Glu Asp Phe Ile Glu Leu Cys Thr  
 275 280 285  
 Pro Gly Val Ile Lys Gln Glu Lys Leu Gly Thr Val Tyr Cys Gln Ala  
 290 295 300  
 Ser Phe Pro Gly Ala Asn Ile Ile Gly Asn Lys Met Ser Ala Ile Ser  
 305 310 315 320  
 Val His Gly Val Ser Thr Ser Gly Gly Gln Met Tyr His Tyr Asp Met  
 325 330 335  
 Asn Thr Ala Ser Leu Ser Gln Gln Gln Asp Gln Lys Pro Ile Phe Asn  
 340 345 350  
 Val Ile Pro Pro Ile Pro Val Gly Ser Glu Asn Trp Asn Arg Cys Gln  
 355 360 365  
 Gly Ser Gly Asp Asp Asn Leu Thr Ser Leu Gly Thr Leu Asn Phe Pro  
 370 375 380



Gly	Arg	Thr	Val	Phe	Ser	Asn	Gly	Tyr	Ser	Ser	Pro	Ser	Met	Arg	Pro
385					390					395					400
Asp	Val	Ser	Ser	Pro	Pro	Ser	Ser	Ser	Ser	Thr	Ala	Thr	Thr	Gly	Pro
				405					410					415	
Pro	Pro	Lys	Leu	Cys	Leu	Val	Cys	Ser	Asp	Glu	Ala	Ser	Gly	Cys	His
			420					425					430		
Tyr	Gly	Val	Leu	Thr	Cys	Gly	Ser	Cys	Lys	Val	Phe	Phe	Lys	Arg	Ala
		435					440					445			
Val	Glu	Gly	Gln	His	Asn	Tyr	Leu	Cys	Ala	Gly	Arg	Asn	Asp	Cys	Ile
	450					455					460				
Ile	Asp	Lys	Ile	Arg	Arg	Lys	Asn	Cys	Pro	Ala	Cys	Arg	Tyr	Arg	Lys
465					470					475					480
Cys	Leu	Gln	Ala	Gly	Met	Asn	Leu	Glu	Ala	Arg	Lys	Thr	Lys	Lys	Lys
				485					490					495	
Ile	Lys	Gly	Ile	Gln	Gln	Ala	Thr	Thr	Gly	Val	Ser	Gln	Glu	Thr	Ser
			500					505					510		
Glu	Asn	Pro	Gly	Asn	Lys	Thr	Ile	Val	Pro	Ala	Thr	Leu	Pro	Gln	Leu
		515					520					525			
Thr	Pro	Thr	Leu	Val	Ser	Leu	Leu	Glu	Val	Ile	Glu	Pro	Glu	Val	Leu
	530					535					540				
Tyr	Ala	Gly	Tyr	Asp	Ser	Ser	Val	Pro	Asp	Ser	Thr	Trp	Arg	Ile	Met
545					550					555					560
Thr	Thr	Leu	Asn	Met	Leu	Gly	Gly	Arg	Gln	Val	Ile	Ala	Ala	Val	Lys
				565					570					575	
Trp	Ala	Lys	Ala	Ile	Pro	Gly	Phe	Arg	Asn	Leu	His	Leu	Asp	Asp	Gln
			580					585					590		
Met	Thr	Leu	Leu	Gln	Tyr	Ser	Trp	Met	Phe	Leu	Met	Ala	Phe	Ala	Leu
		595					600					605			
Gly	Trp	Arg	Ser	Tyr	Arg	Gln	Ser	Ser	Ala	Asn	Leu	Leu	Cys	Phe	Ala
	610					615					620				
Pro	Asp	Leu	Ile	Ile	Asn	Glu	Gln	Arg	Met	Thr	Leu	Pro	Cys	Met	Tyr
625					630					635					640
Asp	Gln	Cys	Lys	His	Met	Leu	Tyr	Val	Ser	Ser	Glu	Leu	His	Arg	Leu
				645					650					655	
Gln	Val	Ser	Tyr	Glu	Glu	Tyr	Leu	Cys	Met	Lys	Thr	Leu	Leu	Leu	Leu
			660					665					670		
Ser	Ser	Val	Pro	Lys	Asp	Gly	Leu	Lys	Ser	Gln	Glu	Leu	Phe	Asp	Glu
		675					680						685		

Ile Arg Met Thr Tyr Ile Lys Glu Leu Gly Lys Ala Ile Val Lys Arg  
690 695 700

Glu Gly Asn Ser Ser Gln Asn Trp Gln Arg Phe Tyr Gln Leu Thr Lys  
705 710 715 720

Leu Leu Asp Ser Met His Glu Val Val Glu Asn Leu Leu Asn Tyr Cys  
725 730 735

Phe Gln Thr Phe Leu Asp Lys Thr Met Ser Ile Glu Phe Pro Glu Met  
740 745 750

Leu Ala Glu Ile Ile Thr Asn Gln Ile Pro Lys Tyr Ser Asn Gly Asn  
755 760 765

Ile Lys Lys Leu Leu Phe His Gln Lys  
770 775

<210> 14  
<211> 933  
<212> PRT  
<213> Homo sapiens

<220>  
<221> DOMAIN  
<222> (659)..(918)  
<223> minimal ligand binding domain

<400> 14

Met Thr Glu Leu Lys Ala Lys Gly Pro Arg Ala Pro His Val Ala Gly  
1 5 10 15

Gly Pro Pro Ser Pro Glu Val Gly Ser Pro Leu Leu Cys Arg Pro Ala  
20 25 30

Ala Gly Pro Phe Pro Gly Ser Gln Thr Ser Asp Thr Leu Pro Glu Val  
35 40 45

Ser Ala Ile Pro Ile Ser Leu Asp Gly Leu Leu Phe Pro Arg Pro Cys  
50 55 60

Gln Gly Gln Asp Pro Ser Asp Glu Lys Thr Gln Asp Gln Gln Ser Leu  
65 70 75 80

Ser Asp Val Glu Gly Ala Tyr Ser Arg Ala Glu Ala Thr Arg Gly Ala  
85 90 95

Gly Gly Ser Ser Ser Ser Pro Pro Glu Lys Asp Ser Gly Leu Leu Asp  
100 105 110

Ser Val Leu Asp Thr Leu Leu Ala Pro Ser Gly Pro Gly Gln Ser Gln  
115 120 125

Pro Ser Pro Pro Ala Cys Glu Val Thr Ser Ser Trp Cys Leu Phe Gly  
130 135 140



Ser Ser Ala Ser Ser Ser Gly Ser Thr Leu Glu Cys Ile Leu Tyr Lys  
 450 455 460  
 Ala Glu Gly Ala Pro Pro Gln Gln Gly Pro Phe Ala Pro Pro Pro Cys  
 465 470 475 480  
 Lys Ala Pro Gly Ala Ser Gly Cys Leu Leu Pro Arg Asp Gly Leu Pro  
 485 490 495  
 Ser Thr Ser Ala Ser Ala Ala Ala Gly Ala Ala Pro Ala Leu Tyr  
 500 505 510  
 Pro Ala Leu Gly Leu Asn Gly Leu Pro Gln Leu Gly Tyr Gln Ala Ala  
 515 520 525  
 Val Leu Lys Glu Gly Leu Pro Gln Val Tyr Pro Pro Tyr Leu Asn Tyr  
 530 535 540  
 Leu Arg Pro Asp Ser Glu Ala Ser Gln Ser Pro Gln Tyr Ser Phe Glu  
 545 550 555 560  
 Ser Leu Pro Gln Lys Ile Cys Leu Ile Cys Gly Asp Glu Ala Ser Gly  
 565 570 575  
 Cys His Tyr Gly Val Leu Thr Cys Gly Ser Cys Lys Val Phe Phe Lys  
 580 585 590  
 Arg Ala Met Glu Gly Gln His Asn Tyr Leu Cys Ala Gly Arg Asn Asp  
 595 600 605  
 Cys Ile Val Asp Lys Ile Arg Arg Lys Asn Cys Pro Ala Cys Arg Leu  
 610 615 620  
 Arg Lys Cys Cys Gln Ala Gly Met Val Leu Gly Gly Arg Lys Phe Lys  
 625 630 635 640  
 Lys Phe Asn Lys Val Arg Val Val Arg Ala Leu Asp Ala Val Ala Leu  
 645 650 655  
 Pro Gln Pro Leu Gly Val Pro Asn Glu Ser Gln Ala Leu Ser Gln Arg  
 660 665 670  
 Phe Thr Phe Ser Pro Gly Gln Asp Ile Gln Leu Ile Pro Pro Leu Ile  
 675 680 685  
 Asn Leu Leu Met Ser Ile Glu Pro Asp Val Ile Tyr Ala Gly His Asp  
 690 695 700  
 Asn Thr Lys Pro Asp Thr Ser Ser Ser Leu Leu Thr Ser Leu Asn Gln  
 705 710 715 720  
 Leu Gly Glu Arg Gln Leu Leu Ser Val Val Lys Trp Ser Lys Ser Leu  
 725 730 735  
 Pro Gly Phe Arg Asn Leu His Ile Asp Asp Gln Ile Thr Leu Ile Gln  
 740 745 750





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Ala	Gln	Glu	Val	Pro	Phe	Pro	Lys	Thr	Glu	Glu	Val	Glu	Ser	Ala	Ile	
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Glu	Pro	Asp	Gly	Ala	Phe	Ser	Ser	Ser	Cys	Leu	Gly	Gly	Asn	Ser	Lys	
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Ile	Asn	Ser	Asp	Ser	Ser	Phe	Ser	Val	Pro	Ile	Lys	Gln	Glu	Ser	Thr	
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Pro	Phe	Pro	Phe	Met	Asp	Gly	Ser	Tyr	Phe	Ser	Phe	Met	Asp	Asp	Lys	
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Asp	Tyr	Tyr	Ser	Leu	Ser	Gly	Ile	Leu	Gly	Pro	Pro	Val	Pro	Gly	Phe	
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Asp	Gly	Asn	Cys	Glu	Gly	Ser	Gly	Phe	Pro	Val	Gly	Ile	Lys	Gln	Glu	
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Pro	Asp	Asp	Gly	Ser	Tyr	Tyr	Pro	Glu	Ala	Ser	Ile	Pro	Ser	Ser	Ala	
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Gln	His	Leu	Ser	Ser	Phe	Pro	Pro	Val	Asn	Thr	Leu	Val	Glu	Ser	Trp	
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Lys	Ser	His	Gly	Asp	Leu	Ser	Ser	Arg	Arg	Ser	Asp	Gly	Tyr	Pro	Val	
565							570					575				
Leu	Glu	Tyr	Ile	Pro	Glu	Asn	Val	Ser	Ser	Ser	Thr	Leu	Arg	Ser	Val	
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Ser	Thr	Gly	Ser	Ser	Arg	Pro	Ser	Lys	Ile	Cys	Leu	Val	Cys	Gly	Asp	
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Gly	Arg	Asn	Asp	Cys	Ile	Ile	Asp	Lys	Ile	Arg	Arg	Lys	Asn	Cys	Pro	

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Pro	Gln	Gln	Gln	Gln	Pro	Pro	Pro	Pro	Pro	Pro	Pro	Pro	Gln	Ser	Pro																								
690										695										700																			
Glu	Glu	Gly	Thr	Thr	Tyr	Ile	Ala	Pro	Ala	Lys	Glu	Pro	Ser	Val	Asn																								
705										710										715										720									
Thr	Ala	Leu	Val	Pro	Gln	Leu	Ser	Thr	Ile	Ser	Arg	Ala	Leu	Thr	Pro																								
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785										790										795										800									
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Asp	Ser	Met	His	Asp	Leu	Val	Ser	Asp	Leu	Leu	Glu	Phe	Cys	Phe	Tyr																								
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Thr	Phe	Arg	Glu	Ser	His	Ala	Leu	Lys	Val	Glu	Phe	Pro	Ala	Met	Leu																								





Thr Val Ser His Ile Glu Gly Tyr Glu Cys Gln Pro Ile Phe Leu Asn  
 195 200 205  
 Val Leu Glu Ala Ile Glu Pro Gly Val Val Cys Ala Gly His Asp Asn  
 210 215 220  
 Asn Gln Pro Asp Ser Phe Ala Ala Leu Leu Ser Ser Leu Asn Glu Leu  
 225 230 235 240  
 Gly Glu Arg Gln Leu Val His Val Val Lys Trp Ala Lys Ala Leu Pro  
 245 250 255  
 Gly Phe Arg Asn Leu His Val Asp Asp Gln Met Ala Val Ile Gln Tyr  
 260 265 270  
 Ser Trp Met Gly Leu Met Val Phe Ala Met Gly Trp Arg Ser Phe Thr  
 275 280 285  
 Asn Val Asn Ser Arg Met Leu Tyr Phe Ala Pro Asp Leu Val Phe Asn  
 290 295 300  
 Glu Tyr Arg Met His Lys Ser Arg Met Tyr Ser Gln Cys Val Arg Met  
 305 310 315 320  
 Arg His Leu Ser Gln Glu Phe Gly Trp Leu Gln Ile Thr Pro Gln Glu  
 325 330 335  
 Phe Leu Cys Met Lys Ala Leu Leu Leu Phe Ser Ile Ile Pro Val Asp  
 340 345 350  
 Gly Leu Lys Asn Gln Lys Phe Phe Asp Glu Leu Arg Met Asn Tyr Ile  
 355 360 365  
 Lys Glu Leu Asp Arg Ile Ile Ala Cys Lys Arg Lys Asn Pro Thr Ser  
 370 375 380  
 Cys Ser Arg Arg Phe Tyr Gln Leu Thr Lys Leu Leu Asp Ser Val Gln  
 385 390 395 400  
 Pro Ile Ala Arg Glu Leu His Gln Phe Thr Phe Asp Leu Leu Ile Lys  
 405 410 415  
 Ser His Met Val Ser Val Asp Phe Pro Glu Met Met Ala Glu Ile Ile  
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 Ser Val Gln Val Pro Lys Ile Leu Ser Gly Lys Val Lys Pro Ile Tyr  
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